

REFERENCES

1. Terranova G, Ferro M, Carpeggiani C, et al. Low quality and lack of clarity of current informed consent forms in cardiology: how to improve them. *J Am Coll Cardiol Img* 2012;5:649–55.
2. Gould KL, Pan T, Lohin C, Johnson NP, Guha A, Sdringola S. Frequent diagnostic errors in cardiac PET/CT due to misregistration of CT attenuation and emission PET images: a definitive analysis of causes, consequences, and corrections. *J Nucl Med* 2007;48:1112–21.
3. Gould KL, Pan T, Lohin C, Johnson NP, Sdringola S. Reducing radiation dose in rest-stress cardiac PET/CT by single poststress cine CT for attenuation correction: quantitative validation. *J Nucl Med* 2008;49:738–45.
4. Johnson NP, Gould KL. Physiological basis for angina and ST-segment change PET-verified thresholds of quantitative stress myocardial perfusion and coronary flow reserve. *J Am Coll Cardiol Img* 2011;4:990–8.
5. Picano E, Vano E. The radiation issue in cardiology: the time for action is now. *Cardiovasc Ultrasound* 2011;9:35.
6. Picano E. Stress echocardiography: a historical perspective. *Am J Med* 2003;114:126–30.
7. Picano E. Sustainability of medical imaging. Education and debate. *BMJ* 2004;328:578–80.

REPLY

We thank Drs. Johnson and Gould for their interest in our paper (1). The “factually incorrect” doses reported in Figure 3 are indeed correct. Positron emission tomography (PET) scans are usually coupled with angiogram computed tomography (CT) and lead precisely to a cumulative (CT angiogram + PET scan) dose of approximately 20 mSv (1,000 chest x-rays) (2). PET scan alone (without CT) totals 2 mSv with ¹³N-ammonia, and 3 mSv with ⁸²Rb-rubidium. Obviously, reported doses are only reference doses, and lower doses can be achieved with state-of-the-art CT technology. On the other hand, for each test (from CT to single-photon emission computed tomography [SPECT] to coronary angiography), substantially (up to 5-fold) higher doses can be recorded in the real world—especially when no systematic dose audit is implemented in the imaging laboratory (3).

We agree that a major advantage of PET myocardial perfusion imaging is the lower radiation dose when compared with SPECT (2 mSv vs. 8 to 10 mSv). Obviously, this advantage may apply mainly in cost-insensitive settings in which there is no technology or expertise for zero-dose cardiac testing with magnetic resonance imaging or stress echocardiography—which provide similar diagnostic and prognostic results at much lower cost using radiation-free techniques (4). Only an explicit, systematic discussion of costs and risks would facilitate the identification of appropriate, sustainable medical imaging strategies (5), avoiding the use of high-cost, high-risk techniques instead of low-cost, low-risk methods with comparable benefit.

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REFERENCES

1. Terranova G, Ferro M, Carpeggiani C, et al. Low quality and lack of clarity of current informed consent forms in cardiology: how to improve them. *J Am Coll Cardiol Img* 2012;5:649–55.
2. Kajander S, Joutsiniemi E, Saraste M, et al. Cardiac positron emission tomography/computed tomography imaging accurately detects anatomically and functionally significant coronary artery disease. *Circulation* 2010;122:603–13.

Intraplaque Hemorrhage, RBC-Derived Cholesterol, and Plaque Progression

Time to Move From Conjecture to Evidence?

The interesting study by Sun et al. (1) in a recent issue of *JACC* adds important new insights into the role of intraplaque hemorrhage (IPH) in the natural history of carotid atherosclerosis. Serial magnetic resonance imaging (MRI) over an extended period of observation demonstrated that plaque growth after the occurrence of IPH was on average higher compared with the period before IPH (1). Notably, however, the rate of individual plaque growth differed substantially after the occurrence of IPH; some plaques actually showed regression despite evidence of new IPH, as shown in Figure 4 of Sun et al. (1). Thus, this study strongly links IPH to accelerated atherosclerosis, but it also raises a key issue: detection of IPH alone may be a suboptimal predictor of the exact rate and magnitude of subsequent plaque growth. Therefore, identification of other factors that modulate the proatherogenic effect of IPH might enhance the potential of MRI to accurately predict which lesions with IPH will exhibit most pronounced and rapid growth. Based on the pathobiological sequelae of IPH (2), we suggest that differences in the cholesterol contents of erythrocyte membranes (CEM) are very likely to account, at least in part, for the observed differential plaque growth after IPH (1).

The driving mechanisms of plaque progression and the main source of cholesterol that is accumulated in the developing plaque differ fundamentally in lesions without versus those with IPH. In lesions without IPH, cholesterol in the plaque is derived mainly from circulating blood lipoproteins; hence, higher blood cholesterol levels amplify the proatherogenic stimulus of adverse local hemodynamics, which is a major driving force of focal plaque development in this setting (3). In contrast, in lesions with IPH extravasated erythrocytes contain abundant free cholesterol that is absorbed into the necrotic core and is conjectured to contribute centrally to plaque enlargement (2). Accordingly, in lesions with IPH, it seems highly plausible that increasing levels of CEM might amplify the proatherogenic stimulus of IPH per se.

Of clinical importance, the CEM can be measured in the clinic (4,5) and is positively related to coronary plaque burden (4) and plaque instability (5). We hereby propose that the combination of CEM measurement with serial MRI may substantiate our current understanding of the role of IPH in plaque biology and, consequently, may enhance risk-stratification of patients with evidence of IPH. First, a finding of greatest plaque progression after IPH in patients with higher compared with those with lower CEM levels would lend definitive mechanistic support to the long-standing